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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,468	04/02/2001	Arthur M. Krieg	C1039/7049(HCL/MAT)	9046

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/824,468	KRIEG ET AL.	
	Examiner	**Art Unit**	
	Terra C. Gibbs	1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 October 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *22-43*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *See Continuation Sheet*

Continuation of 5. does NOT place the application in condition for allowance because: Claims 22-43 remain rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants argue Broide et al. is not relevant to the evaluation of the present claims under 35 U.S.C. §112 because the teachings of Broide et al. relate to the administration of an immunostimulatory DNA alone and not in combination with an immunopotentiating cytokine. This is not found persuasive because the claims recite a method for inducing a synergistic antigen specific immune response comprising the administration of an immunopotentiating cytokine such as IL-3 and an immunostimulatory CpG oligonuceltide. Broide et al. disclose the inhibition of IL-3 secretion following i.p. injection of an immunostimulatory DNA (see Table 1). Therefore it is unclear how the administration of IL-3 and an immunostimulatory CpG oligonucletoide will induce a synergistic antigen specific immune response as contemplated in the claims where immunostimulatory CpG oligonucleotides antagonize cytokine secretion. Applicants contend that the disclosure of Broide et al. would not cause one of skill in the art to doubt the teachings of the instant application. Applicants rely on Exhibit 1 and a Declaration under 37 CFR §1.132 to describe the results of several experiments that demonstrate the successful synergistic stimulation of an immune cell response in the presence of a CpG oligonucleotide in combination with either IL-3 or IL-12. This is not found persuasive because Applicants Exhibit 1 and Declaration under 37 CFR §1.132 have not been considered because there is no apparent reason why Exhibit 1 and the Declaration under 37 CFR §1.132 were not presented earlier during prosecution of the instant application.

Continuation of 10. Other: Claims 22-43 remain rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The instant specification teaches the combination of GM-CSF and CpG phosphorothioated oligonucleotide 2006 shows synergy for increasing the expression of CD86 and CD40 molecule expression on dendritric cells (see Figure 9). The claims contemplate the use of IL-3 and IL-12 as inducers of immune response synergism in a subject in combination with a CpG oligonucleotide However, the instant specification as filed does not teach how the skilled artisan would use IL-3 and IL-12 as an inducer of immune response synergism in a subject in combination with a CpG oligonucleotide, given the results of Broide et al. which disclosed that an immunostimulatory DNA containing a CpG motif inhibited IL-3 production in mice. Applicants now rely on Exhibit 1 and a Declaration under 37 CFR §1.132 to describe the results of several experiments that demonstrate the successful synergistic stimulation of an immune cell response in the presence of a CpG oligonucleotide in combination with either IL-3 or IL-12. However, Applicants Exhibit 1 and Declaration under 37 CFR §1.132 have not been considered because there is no apparent reason why Exhibit 1 and the Declaration under 37 CFR §1.132 were not presented earlier during prosecution of the instant application. One skilled in the art would not accept on its face the examples given in the specification of the synergism elicited by CpG phosphorothioated oligonucleotide 2006 and the cytokine GM-CSF as being correlative or representative of the induction of immune response synergism in a subject in combination with a CpG oligonucleotide and IL-3 and IL-12. Therefore, in view of the lack of guidance in the specification regarding the use of IL-3 and IL-12 as inducers of immune response synergism in a subject in combination with a CpG oligonucleotide, and the unpredictability associated with immunostimulatory DNA containing CpG motifs as antagonistic agents against IL-3 production in mice, undue experimentation would be required. Therefore, practice of the full scope of the invention would require undue experimentation.

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER